REMARKS/ARGUMENTS

In response to the Requirements for Patent Applications Containing Nucleotide and/or Amino Acid Sequence Disclosures/Notice please find enclosed a Sequence Listing that reflects the sequences set forth in the Specification as originally filed. This amendment and response does not incorporate any new matter. A diskette with the Sequence Listing is attached and consideration of the application is requested. The sequence listing information recorded in computer readable form is identical to the written Sequence Listing as required under 37 C.F.R. 1.821(b). The Applicant submits that the Sequence Listing is fully compliant with the requirements of the rules (37 C.F.R. 1.821-1.825). The Applicant respectfully requests entry of the Sequence Listing.

In response to the final restriction requirement, Applicant has withdrawn the non-elected claims, namely, claims 44-86. The limitation of claim 45 has been added to the remaining claims and references to that claim number have been removed. Claims 34-43, 95 and 109-114 remain pending in this application.

Objections

Claims 37, 41, 34-43, 109-113 and 114 are objected to for various informalities. Applicant believes that the claims as amended overcome the objections.

The cross-reference to other applications in the specification has been amended.

Applicant amends herein portions of the text of the application that were objected to, namely, with application serial numbers and ATCC reference numbers, where available.

Rejections

Claims 34-43, 95, 109-114 stand rejected under 35 U.S.C. §112, second paragraph for failure to distinctly point out and claim the invention. Applicant respectfully traverses the rejection.

The Action states that the term "steroid hormone-like" is indefinite in claims 34 and 95 because it is a relative phrase, however, the use of imprecise language does not automatically render claim invalid for indefiniteness, and if term of degree, such as "substantially," is used in claim, then court must determine whether specification provides some standard for measuring that degree, such that one of skill in art would understand what is claimed (Bausch & Lomb Inc. v. Alcon Laboratories Inc., D.C. W.N.Y., 12/22/99, p.1353). In the present case the term "steroid hormone-like" would be interpreted by even a minimally skilled artisan to include those agents that have an effect on cells similar to those of a steroid

hormone. However, the Applicant need not rely on that which is readily apparent to the artisan, the Applicant notes in the application that:

> [0049] Certain embodiments of the present invention provide in vitro assay methods for **detecting steroid hormone-like** cell growth stimulation by a substance of interest. In some embodiments, the **assay method comprises maintaining a predetermined population of steroid hormone-responsive cells in a nutrient medium comprising a quantity of an immunoglobulin cell growth inhibitor sufficient to inhibit cell growth in the absence of an inhibition-reversing amount of the steroid hormone**. In some embodiments **the medium is serum-free** and **the cells themselves are serum free** and **obtained from a stable steroid hormone-responsive cell line**. The method also comprises adding a substance of interest to the cells and medium to yield a test mixture. The test mixture is then incubated for a predetermined period of time under cell growth promoting conditions. "Cell growth promoting conditions" refer to general environmental conditions, other than defined medium components, and include such things as favorable conditions of gaseous atmosphere, temperature and pH. For example, cell growth promoting conditions could include incubation at 37°C in a humid atmosphere of 5% (v/v) CO2 and 95% (v/v) air in a defined nutrient medium at pH 7.4. After incubation for the desired period of time, it is determined whether the cell population in the test mixture has measurably increased, an increase indicating a steroid hormone-like cell growth stimulating effect by the substance of interest. An assay procedure such as this can be used for in vitro screening of drugs or other body-affecting substances for unwanted cell growth stimulating properties as an aid to avoiding undesirable side effects of such drug or substance in vivo. In certain alternative embodiments, the assay method includes adding to the nutrient medium a defined amount of steroid-hormone depleted serum, which contains the inhibitor(s), and which is obtained from non-heat inactivated serum. (Emphasis added).

Clearly, the skilled artisan could take well-known steroid responsive cells and grow them in accordance with the conditions and the various media as skillfully taught in the present specification to determine, with minimal skill, a "steroid-like effect" on the cells. In fact, the task of testing for steroid-like effects is easily taught to a skilled technician for application and determination.

Furthermore, Example 15 teaches the use of an inhibitor depleted medium of the present invention that can be used to test compounds that might possess cytotoxic activity independent of any steroid hormone-like cell growth stimulating ("steroidogenic") effects or other hormone-like properties. The methods described permit assays for commercial, environmental, industrial and medical compounds, substances and mixtures for inhibitor-like activity and/or cytotoxic activity in the same preparations. Therefore, the specification not only teaches how the skilled would test for the effect but also how and with what it may find particular uses.

Finally, as regards the usage of the phrase "steroid hormone-like" a simple GOOGLE search on the exact words of the phrase in the art yields over 219 hits. Within GOOGLE SCHOLAR, at least 14 scientific

publications include the exact phrase. While "androgenic" and "estrogenic" may be believed to be inconsistently used by two references, it is clear that the scientific community understands and uses the phrase with some regularity. For example, in the Journal of Mutagenesis investigators from U. of California-San Francisco as well as Deakin University in Australia use the phrase in the title of an article entitled, "Environmental factors affecting transcription of the human L1 retrotransposon. I. **Steroid hormone-like agents**" Mutagenesis, Vol. 17, No. 3, 193-200, May 2002 (emphasis added).

Interestingly, the inventors of the 5,135,849 patent themselves (Sonnenschein C, Soto AM) refer to agents that have a "hormone-like" effect in their article entitled "An updated review of environmental estrogen and androgen mimics and antagonists." J Steroid Biochem Mol Biol. 1998 Apr;65(1-6):143-50. ("...substantial evidence has surfaced on the hormone-like effects of environmental chemicals such as pesticides and industrial chemicals in wildlife and humans." Abstract). The '849 claims also include the terminology "substance of interest," which has been provided the imprimatur of the Patent Office. Therefore, the artisans that are cited to reject the present claims (infra) use not only the term "hormone-like," but also the term "substance of interest." The evidence of record demonstrates that the skilled artisan recognizes the terms used in the present claims. Finally, a search of PTO database, searching in the claims only, shows that at least 15 patents have issued in the United States that include the term "hormone-like." As such, the Applicant believes that the rejection has been overcome and respectfully requests withdrawal of the rejection.

As regards the term "substantially devoid," the law is simple, the use of imprecise language does not automatically render claim invalid for indefiniteness, and if term of degree, such as "substantially," is used in claim, then court must determine whether specification provides some standard for measuring that degree, such that one of skill in art would understand what is claimed (*Bausch & Lomb Inc. v. Alcon Laboratories Inc.*, D.C. W.N.Y., 12/22/99, p.1353). The term devoid is well-known to mean empty or lacking, therefore, substantially devoid would be understood by the skilled artisan to mean "substantially free" of the unbound iron. Applicant would be glad to amend the claims to use the phrase "substantially free" as used in the claims of U.S. Patents 6,123,938 and 6,497,881; if that will lead to withdrawal of the rejection. As such, the Applicant believes that the rejection has been overcome and respectfully requests withdrawal of the rejection.

Claims 34-39, 41-43, 95, 109-114 stand rejected under 35 USC §112, first paragraph, for lack of enablement. Applicant respectfully traverses the rejection.

The arguments and evidence that pertain to the indefiniteness rejection are incorporated herein by

reference. Applicant traverses the rejection because the specification provides extensive discussion, examples, figures and data to support enablement for the method claims at issue in this Action. The Action argues that the art recognizes the existence of long-standing problems that need to be solved and that the specification fails to provide sufficient structures and/or that only a few examples are shown. As discussed in detail hereinbelow, at issue are method claims that are used to examine "substances of interest," support for which has been discussed hereinabove.

The discussion of *Rochester v. Searle* 358 F.3d 916 (Fed. Cir. 2004), in inapposite to the present claims. The University of Rochester's claims were reach-through claims, that is, product by process claims. The claims at issue are method claims. Its relevance, if any, is further lessened by the simple fact that several examples of the immunoglobulin inhibitors that may be used with the method are taught and their effects clearly demonstrated. It has already been established, supra, that steroid-like effects and agents are well known, therefore, the method of the present invention clearly provides enablement for a method of screening for agents with these steroid-like effect in conjunction with the novel immunoglobulin inhibitors. In the present claims no such agent is claimed per se, as was the case with the claims at issue in *Rochester*, therefore, the case law cited is not applicable to the claims at issue.

When investigating or attempting to reach a substance of interest, the skilled artisan would know to use any of a number of chemical libraries, pools of libraries and the like. The relevant case law is whether it is necessary for the specification to provide every modification and configuration. It is not. (See, e.g., *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991) (Furthermore, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted)). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further, the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). In the present invention the key enabling agent is the inhibitory immunoglobulin that enables the method that is used to examine the potential substance of interest.

The Action in pages 9 - 15 raises a number of points that lead to the discussion and rejection based on the *Rochester* case. As it has been demonstrated that the Rochester case is not on point, addressing each and every part of the syllogism that leads to the rejection is not necessary.

Regardless, the Applicant does not agree with certain characterizations in the Action. On page 12, the Action makes the assumption that because data was not shown for IgG2-kappa and that its discussion was not followed up in the Example 23 that somehow its effect was not significant. Applicant

strongly disagrees and traverses any such assumptions and implications. The best evidence of the meaning of the specification is the specification itself. The specification teaches and constructively reduces to practice the invention as stated.

Also, on pages 12-13, a statement is made that:

> One cannot extrapolate the teaching of the specification to the enablement of the claims because the specification clearly and repeatedly teaches that the identification of the immunoglobulin inhibitors was a "surprising" [sic] that is, an unexpected event and that fifteen years of combined research by those skilled in the art failed to identify serum-borne inhibitors of steroid responsive cell growth despite its first proposal more that fifteen years ago, the purified reversible serum-borne inhibitors had not been previously described.

If the office has caselaw that it wishes to present for that proposition, that is, that "one cannot extrapolate from the specification to the enablement of the claims," Applicant stands ready to traverse and address any such caselaw when presented.

On page 13 there is also a scientific discussion of the nature and scope of the types of Fc receptors that may or may not bind the immunoglobulin inhibitors of the present invention, arguing that their exact nature and structure must be provided and that certain immunoglobulin light chains might be preferred. While certain Fc receptors might bind certain light chains with a certain preference, Applicants assert that any such "preference" is not that of the Applicant and all equivalent Fc receptors fall within the scope of the claims. Finally, if a specific claim is at issue, the Applicant respectfully request a rejection based on those one or more claims to which the discussion is pertinent or withdrawal of the rejection.

On page 14 the new "extrapolation" test is one again stated in the context of the immunoglobulin inhibitors. The immunoglobulin inhibitors, how they are obtained, isolated, characterized and used is taught for not one, but four species, horse, rat, mouse and human as shown in figures 98-148. At the end of page 14 there is also the statement that, "[i]t is clear that in the absence of an effective steroid reversible inhibitor, one would not be able to successfully use the claimed broadly claimed [sic] invention." But such an inhibitor is taught, therefore the statement is not applicable to the present invention.

Finally, on page 15 the assumptions, statements, extrapolations, appearances and conclusions, what are respectfully traversed, lead to the Action's statement that "no working example," are provided by the application. Applicant strongly, but respectfully, disagrees. The specification provides 148 figures and 28 examples in 814 paragraphs that support the method that is claimed and rejected in this Action. But bulk alone does not enablement provide. The specification is not merely fluff to be discounted based

on the "lack of predictability" and "failure to reasonably expect success." The present specification provides specific examples, for multiple species, of the inhibitory effect of certain specific inhibitory immunoglobulins that are isolated by specific methods and tested for activity in the particular ways described and claimed. For example, the immunoglobulins are characterized, fractioned, isolated and used in well-recognized, well-characterized and accepted in vitro model systems in both serum and serum-free media with numerous cell types. These techniques are used in novel ways and combinations to arrive at the invention as claimed. As such, the Applicant believes that the rejection has been overcome and respectfully requests withdrawal of the rejection.

Claims 34-39, 41-43, 95, 109-114 stand rejected under 35 USC §112, first paragraph, for lack of sufficient written description. Applicant respectfully traverses the rejection.

The arguments and evidence presented hereinabove is also incorporated herein by reference, as lack of written description rejections often overlap with the common nucleus of facts addressed in response to enablement rejections.

An enabling written description at the time of filing is essential in order to show that the inventor was in "possession" of the claimed invention as of the filing date, which, lacking an earlier verifiable date of conception and reduction to practice, is the constructive date of invention. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). The Federal Circuit has held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." See, e.g., *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Supporting the enablement rejection, the Action cites to two DNA cases, *Eli Lilly* and *Enzo* to find support for a rejection. The conclusion of law in those cases relates to whether the structure, formula or chemical name for broadly claimed (all species) isolated and purified nucleic acids were taught. The claims at issue in the present invention are method claims, therefore, *Eli Lilly* and *Enzo* simply do not apply.

After citing the two DNA cases, the action states that "[a] disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product." Again, the Applicant respectfully requests that the office provide the case law that supports this novel test or requests withdrawal of the rejection. The claims presently at issue are method claims that may be used to test "substances of interest," a phrase that was established, supra, has received the imprimatur of the office. If that is not the case, the Applicant respectfully challenges the office to, sua sponte, withdraw

any such patent from issue (including U.S. Patent 5,738,984, which issued after the *Eli Lilly* and *Enzo* decisions).

On page 18-19, the Applicant notes and appreciates the Action's statement favoring compact prosecution, however, the proposed claim language is stated to still be rejected under 112 for lack of indefiniteness, enablement and written description. As regards compact prosecution, the Applicant's counsel states for the record that on or about December 1, 2005, Applicant's counsel contacted the Examiner regarding the spirit of compact prosecution requesting that the Action be reissued rather than allowing this application to go abandoned because Applicant and Counsel never received the Office Action of March 3, 2005. The Examiner stated that the Office had complied with its single attempt to send the application and was unwilling to re-issue the Action. The Examiner's failure to grant the Applicant's request has extended, rather than compacted prosecution.

On page 21 of the Action, after an extended recitation of some of the novelty and improvements that the present invention provides to the known arts, the new "extrapolation" test is once again applied to the present claims. However, the nature, scope and tenor of the extrapolation test is, if applicable, an enablement rejection, not a written description rejection. The discussion bleeds into page 22 and 23 are regards the use of certain serum-free media. The claims as amended include as a limitation such media, therefore, the basis of the rejection has been addressed.

As such, the specification satisfies the written description requirement under 35 U.S.C. § 112, first paragraph. For the reasons mentioned above, the Applicant respectfully requests the Examiner withdraw the rejection under 35 U.S.C. § 112.

Claims 34-42, 95, 109-114 stand rejected under 35 USC §102 for anticipation in light of U.S. 5,135,849 ('849 patent). Applicant respectfully traverses the rejection.

In order for a rejection under 35 U.S.C. 102(b) to be proper, the cited reference must teach each and every aspect of the claimed invention either explicitly or impliedly. See MPEP §2131. As elaborated in *Richardson v. Suzuki Motor Co.* "[t]he identical invention must be shown in as complete detail as is contained in the claim." 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1987)(see also, *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990), "For a prior art reference to anticipate in terms of 35 USC §102, every element of the claimed invention must be identically shown in a single reference.").

The '849 patent fails to teach and/or claim any immunoglobulin inhibitor, therefore the art fails at anticipate. There is not a single teaching of any immunoglobulin fractionation and/or fraction. In fact,

the specification of the '849 patent does not even include the words: immunoglobulin, antibody, IgA, IgG or IgM. As such, alone or even in combination with other art the '849 patent fails to teach the present invention as claimed.

In fact, the Action states that "the prior art specification does not specifically teach that the inhibitor comprises immunoglobulins," however, the Action also argues that the media contains serum therefore at least a fraction of that is immunoglobulin. Applicant has amended the claims to include the term "isolated" as regards the immunoglobulin inhibitor such that at least one isolation step is required between pure serum and the claimed invention. Support for the language is found in the various types of purifications taught in the specification and as known to the minimally skilled in the art.

For the reasons mentioned above, the art cited fails as prior art. The Applicant respectfully requests the Examiner withdraw the rejection under 35 U.S.C. § 102.

Conclusion

In light of the Amendments and argument, Applicant respectfully submits that the present application is now in condition for allowance. Favorable reconsideration of the application is respectfully requested.

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

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Respectfully submitted,

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